Office Action Dated: February 19, 2009 Docket No: ISIS-5300

Serial No: 10/701,265

1-119. (canceled)

120. (Currently amended) A composition comprising a duplex consisting of a first chemically synthesized oligomeric compound oligonucleotide and a second chemically synthesized oligomeric compound oligonucleotide, wherein:

each of the first chemically synthesized oligomeric compound oligonucleotide and the second chemically synthesized oligomeric compound oligonucleotide independently consists of 17 to 25 linked nucleosides, each nucleoside comprising a nucleobase and a sugar;

the first chemically synthesized oligomeric compound <u>oligonucleotide</u> is 100% complementary to the second chemically synthesized oligomeric compound <u>oligonucleotide</u> and to a target mRNA;

the first chemically synthesized oligomeric compound oligonucleotide and the second chemically synthesized oligomeric compound oligonucleotide are not covalently linked to each other; and

the first chemically synthesized oligomeric compound oligonucleotide is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2'-OH 2'-hydroxy-pentofuranosyl sugar moiety, and wherein each nucleoside of each wing comprises a 2'-sugar modification-or is an LNA nucleoside.

121. (Currently amended) The composition of claim 120, wherein the second chemically synthesized oligomeric compound oligonucleotide is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2' OH 2'-hydroxyl pentofuranosyl sugar moiety, and wherein each nucleoside of each wing comprises a 2' modification or is an LNA nucleoside.

122-123. (Canceled)

124. (Currently amended) The composition of claim 120, wherein each nucleoside of at least one of the wings of the gapmer comprises a 2' sugar modification selected from fluoro, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy or is an LNA nucleoside.

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Serial No: 10/701,265

125-126. (canceled)

127. (Previously presented) The composition of claim 120, wherein each nucleoside of the 3'

wing of the gapmer comprises a 2'- OCH₃.

128-135. (Canceled)

136. (Previously presented) The composition of claim 120, wherein each wing of the gapmer

is from two to seven nucleosides in length.

137. (Currently amended) The composition of claim 120, wherein at least one of the first

chemically synthesized oligomeric compound <u>oligonucleotide</u> and the second chemically

synthesized oligomeric compound oligonucleotide comprises at least one phosphorothioate

linkage.

138. (Currently amended) The composition of claim 137, wherein each of the first chemically

synthesized oligomeric compound oligonucleotide and the second chemically synthesized

oligomeric compound oligonucleotide comprises at least one phosphorothioate linkage.

139-167. (Canceled)

3